Sintilimab 治疗中国复发/难治性经典型霍奇金淋巴瘤：多中心、单臂 II 期 ORIENT-1 研究的长期随访研究

Sintilimab for relapsed/refractory classical Hodgkin’s lymphoma: Long-term follow-up on the multicenter, single-arm phase II ORIENT-1 study.

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背景：在 ORIENT-1 研究的初步分析中发现 Sintilimab（PD-1 抑制剂）已显示出对复发/难治性经典型霍奇金淋巴瘤（R/R cHL）的疗效。在此我们报告了长期随访后治疗安全性和疗效性的更新结果。

方法：ORIENT-1 是一项在中国进行的多中心单臂 II 期研究。入选了包括自体造血干细胞移植（HSCT）在内的≥2 线全身治疗失败的 cHL 患者。每 3 周给予静脉注射 Sintilimab 200mg，直到疾病进展、死亡、出现不可接受的毒性或退出研究为止。主要终点是独立放射学审查委员会（IRRC）根据 IWG 2007 评估的客观缓解率（ORR），此前已有报道；以及 IRRC 随访数据获得的无进展生存期（PFS）。

结果：96 例患者接受了治疗。截至 2019 年 9 月 30 日，有 57.3％的患者完成了为期 2 年的治疗，中位随访时间为 26.7 个月。中位治疗时间为 24.1 个月（范围：0.7 至 24.8）。研究人员发现 49 例疾病进展（PD）的患者中，有 39/49（79.6％）患者接受了超出 PD 的治疗，PD 后中位治疗时间为 8.0 个月（1.4 至 20.8）。PFS 中位数为 18.6 个月（95％CI：14.4 至 22.3）。总体生存中位数尚未达到。2 年的 OS 率为 96.3％（95％CI：88.9％至 98.8％）。在 92/96（95.8％）例患者中报告了与治疗相关的不良事件（TRAE），其中大多数（71/96，74.0％）为 1-2 级。最常见的 3 或 4 级 TRAE 是发热（3/96，3.1％）、脂肪酶增加（3/96，3.1％）和淋巴细胞减少（3/96，3.1％）。

结论：长期的随访结果表明，除了高缓解率外，Sintilimab 还显示出持久的疗效和良好的长期安全性。考虑到超出 PD 的治疗率很高（近 80％），用于评估 PFS 的 IWG 2007 可能不是评估抗 PD-1 抗体在 cHL 中疗效的合格标准。后续还需要进一步的调查和分析。临床试验信息：NCT03114683

原文摘要

Abstract

Background: Sintilimab, a programmed death-1 checkpoint inhibitor, has demonstrated efficacy in relapsed/refractory cHL after the primary

analysis of the ORIENT-1 study. Here, we report the updated safety and efficacy profile after long-term follow-up.

Methods: ORIENT-1 is a multicenter, single-arm, phase II study in China. Classical Hodgkin’s lymphoma patients who had failed ≥2 lines of systemic therapy, including autologous hematopoietic stem cell transplantation (HSCT) were enrolled. Sintilimab, 200 mg IV was given every 3 weeks, until disease progression, death, unacceptable toxicity, or withdrawal from study. The primary endpoint objective response rate (ORR) by an independent radiological review committee (IRRC) per IWG 2007 has been reported before. The progression free survival (PFS) by IRRC follow-up data are reported herein.

Results: 96 patients were treated. As of the data cutoff on 30 Sep, 2019, 57.3 % patients complete two-year treatment, with a median follow-up of 26.7 months. The median duration of treatment was 24.1 months (range: 0.7 to 24.8). Of 49 patients with progressive disease (PD) by investigator, 39/49 (79.6%) patients received treatment beyond PD, with a median treatment duration after PD of 8.0 months (range: 1.4 to 20.8). The median PFS was 18.6 months (95%CI: 14.4 to 22.3). Median overall survival has not been reached. Two-year OS rate was 96.3% (95%CI: 88.9% to 98.8%). The treatment-related adverse event (TRAE) was reported in 92/96 (95.8%) patients, most (71/96, 74.0%) of which were grade 1-2. The most common grade 3 or 4 TRAEs were pyrexia (3/96,

3.1%), lipase increased (3/96, 3.1%) and lymphocyte decreased (3/96, 3.1%).

Conclusions: The results from long-term follow-up showed that, in addition to a high rate of response, sintilimab also demonstrated durable efficacy and favorable long-term safety profile. Considering the high rate (nearly 80%) of treatment beyond PD, IWG 2007 which was used to evaluate PFS may not be a suitable criteria for evaluating the efficacy of anti-PD-1 antibody in cHL. Further investigation and analysis are required.

Clinical trial information: NCT03114683

参考文献：

Su H, Song Y, Jiang W, Sun X, Qian W, Zhang W, Gao Y, Jin Z, Zhou J and Jin C, et al: Sintilimab for relapsed/refractory classical Hodgkin’ s lymphoma: Long-term follow-up on the multicenter, single-arm phase II ORIENT-1 study. J CLIN ONCOL 38: 8034, 2020.